

REMARKS

Claims 1-35 were filed in the original application. Claims 17-21 and 26-35 were cancelled without prejudice, and Claims 36-44 were added, in an amendment mailed August 5, 2002.

In the Office Action of May 6, 2003, the Examiner rejected claims 1-16, 22-25 and 36-44 under 35 U.S.C. 103(a) as being allegedly obvious under McLuen *et al.*, in view of Zuckermann *et al.*

THE CLAIMS ARE NON-OBVIOUS

Applicants assert that the Examiner has not met the burden of establishing a *prima facie* case of obviousness. A *prima facie* case of obviousness requires the Examiner to cite to references that (a) disclose all the elements of the claimed invention, (b) suggest or motivate one of skill in the art to combine or modify those elements to yield the claimed combination, and (c) provide a reasonable expectation of success should the claimed combination be carried out.¹ Failure to establish any one of these three requirements precludes a finding of a *prima facie* case and, without more, entitles Applicants to allowance of the claims at issue. The cited art fails to establish *prima facie* obviousness because the cited references do not teach all of the elements of the claimed invention, and there is no motivation to combine the cited art. Furthermore, even if such a combination were made, the cited art does not teach or suggest every element of the presently claimed invention. Thus, Applicants assert that Claims 1-16, 22-25 and 36-44 are non-obvious over the art cited by the Examiner.

The presently claimed invention comprises a cartridge, for use in an open nucleic acid synthesis system, comprising a plurality of receiving holes configured to hold nucleic acid synthesis columns. The cartridge is further configured to receive one or more O-rings, wherein the presence of the one or more O-rings provides a seal between the nucleic acid synthesis columns and the plurality of receiving holes in the cartridge. This is in contrast to systems that may possess a seal within the nucleic acid synthesis column or vessel itself, as described by

¹ See *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); and *In Re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

Zuckermann *et al.* There are many drawbacks and hazards encountered when using some synthesizers which lack the improvement of the current invention.

One such drawback is column overflow due to inadequate argon pressure. The proper purging of the synthesis columns at each cycle relies on the maintenance of a differential in argon pressure between the top and bottom openings of the columns (*See Specification pages 36-43*). Improper or incomplete purging reduces the efficiency of the synthesis and increases the risk of column overflow. Proper purging depends in part upon the formation of an airtight seal between receiving holes in the cartridge and exterior surfaces of the synthesis columns. The presence of irregularities in the column shape or surface can prevent the formation of an airtight seal, allowing argon to leak around the column exterior, thereby disrupting the pressure differential required to properly purge the columns at each cycle. The need to discard columns having even minor imperfections adds expense to the use of the instrument. If undetected, a faulty seal can lead to poor synthesis and column overflow.

The present invention provides improved synthesizers having reliable seals between the cartridge and the synthesis columns. The present invention provides a number of embodiments of synthesizers having such seals. Thus modified, the cartridge has a greatly improved ability to accommodate imperfections in the exteriors of synthesis columns, and this improvement results in safer, and more efficient and reliable operation of the instrument, with fewer costs associated with chemical spill clean-up, instrument down-time, and the disposal of unusable synthesis columns.

I. The Cited References Do Not Teach or Suggest All of the Elements of the Present Invention

The combination of the cited references do not teach or suggest all the elements of the claimed invention. The Examiner fails to identify a receiving hole in a cartridge, configured to hold an O-ring, and further configured to receive and hold a DNA synthesis column. The Examiner concedes that the primary reference, McLuen *et al.*, does not “teach that the cartridge is configured to receive one or more o-rings to provide the seal between the columns and holes.”² Zuckermann *et al.* is also void of this element.

² Office Action mailed May 6, 2003, page 4.

The cartridge of the present invention comprises a plurality of receiving holes configured to hold DNA synthesis columns, and further configured to receive one or more O-rings. The presence of the O-rings provides a seal between the DNA synthesis column and the receiving holes of the cartridge. Contrary to the Examiner's assertion on page 5 of the Office Action³, Zuckermann *et al.* does not "teach a similar cartridge comprising a plurality of receiving holes configured to hold nucleic acid synthesis columns, wherein the cartridge is further configured to receive an o-ring (i.e. annular sealing means) whereby a seal is formed between the holes and columns." Rather, Zuckermann *et al.* describes the use of an annular sealing device **within** a DNA synthesis column or vessel. The Zuckerman *et al.* reaction vessel, consisting of a container and a valve body, teaches an optional annular sealing means between the elongate conduit portion of the container and valve seat. The annular sealing means thus provides a liquid-tight interface between the conduit and the valve body.⁴

Zuckermann *et al.* teaches that the array of modular reaction vessels is maintained in linear spaced apart relation to each other within a rack having a plurality of receptacles configured to retain the array of reaction vessels.⁵ Zuckermann *et al.* does not teach nor suggest a seal between the reaction vessels and the rack configured to retain the array of reaction vessels. In contrast, the present invention comprises a cartridge, having a plurality of receiving holes configured to hold reaction vessels, which is further configured to receive one or more O-rings.

Neither Zuckermann *et al.* nor McLuen *et al.* teach a cartridge configured to receive one or more O-rings to provide the seal between the reaction columns and receiving holes. Examiner's inability to cite to references that disclose all the elements of the claimed invention causes Examiner's rejection of claims 1-16, 22-25 and 36-44 to fail.

II. There is No Motivation to Combine the References

Claims 1-16, 22-25 and 36-44 are rejected under U.S.C. § 103(a) as being unpatentable over McLuen *et al.* in view of Zuckermann *et al.* Applicants disagree. No motivation to combine these references to arrive at the claimed invention is provided by these references and the Examiner has failed to explain why one of ordinary skill in the art at the time the invention

³ Office Action mailed May 6, 2003, page 5, lines 1-4.

⁴ Zuckermann *et al.*, WO 98/10857, page 11, lines 22-25.

⁵ Zuckermann *et al.*, WO 98/10857, page 13, lines 1-3.

was made would have been motivated to combine these references.⁶ Obviousness cannot be established by combining the teaching of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination.⁷ Applicants assert that the cited references do not contain any suggestion for their combination.

McLuen *et al.* do not identify a problem with forming a seal between the reaction column and the receiving hole of the cartridge. Rather, McLuen *et al.* state that “Preferably, the receiving holes within the cartridge each have a precise diameter for accepting the vials, which also each have a corresponding precise exterior dimension to provide a pressure-tight seal when the vials are inserted into the receiving holes.”⁸ The Examiner argues that “It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the cartridge configuration of McLuen *et al.* by configuring the cartridge to receive o-rings between the holes and columns thereby facilitating a tight seal between the holes and columns as taught by Zuckermann *et al.*” However, as noted above, McLuen *et al.* suggests no problem with forming a seal between the reaction column and the receiving hole of the cartridge and is therefore void of any incentive to look for alternative means to form the seal. The Examiner is reminded that under the law an Examiner is not one skilled in the art and that consequently, the Examiner's opinion as to what one skilled in the art might believe is not sufficient support for a motivation to modify the teachings of the cited reference.⁹

Assuming, *arguendo*, that problems with forming a seal between a reaction column and the receiving hole of the cartridge were perceived, Zuckerman *et al.* does not suggest a seal between the reaction column and the receiving hole of the cartridge. The Examiner alleges that “cartridges configured to receive o-rings thereby providing a seal between holes and columns were well known in the art at the time the claimed invention was made as taught by Zuckermann *et al.* Zuckermann *et al.* teach a similar cartridge comprising a plurality of receiving holes configured to hold nucleic acid synthesis columns, wherein the cartridge is further configured to receive an o-ring (i.e. annular sealing means) whereby a seal is formed between the holes and

⁶ “[W]hen the PTO asserts that there is an explicit or implicit teaching or suggestion in the prior art, it must indicate where such a teaching or suggestion appears.” *In Re Rijckaert*, 9 F.3d 1531; 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); M.P.E.P. at 706.02(j).

⁷ *In Re Geiger*, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987).

⁸ McLuen *et al.*, WO 99/65602, page 7, lines 7-10 and page 12, lines 19-21.

⁹ See, *In re Rijckaert*, 9 F.3d 1531, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993).

columns.¹⁰ Applicants respectfully disagree. Zuckermann *et al.* describes the use of an annular sealing device **within** a DNA synthesis column or vessel. The Zuckerman *et al.* reaction vessel, consisting of a container and a valve body, itself may contain an internal seal between the elongate conduit portion of the container and valve seat. However, there is no teaching or suggestion in Zuckermann *et al.* of a cartridge comprising a plurality of receiving holes configured to hold nucleic acid synthesis columns, wherein the cartridge is further configured to receive an O-ring. Thus, Zuckermann *et al.* do not teach methods relevant to the claimed methods for forming a seal between the receiving hole of a cartridge and the reaction vessel. Therefore, no motivation exists to combine Zuckermann *et al.* with McLuen *et al.*

Furthermore, even if one improperly combined McLuen *et al.* and Zuckermann *et al.*, this combination does not teach or suggest all elements of the presently claimed invention and *prima facie* obviousness is not established. Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicants' claims as amended should be passed to allowance. Should the Examiner have any questions, or if a telephone conference would aid in the prosecution of the present application, Applicant encourages the Examiner to call the undersigned collect at 608-218-6900.

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¹⁰ Office Action mailed May 6, 2003, pages 4-5.